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EXAMINER	
KUMAR, SHAILENDRA	

ART UNIT	PAPER NUMBER
1621	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/575,824	TUCKER, JOHN	
	Examiner	Art Unit	
	SHAILENDRA KUMAR	1621	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 August 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-18* is/are pending in the application.

4a) Of the above claim(s) *13-16* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *9-12,17 and 18* is/are rejected.

7)☒ Claim(s) *1-8* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/GB/08) Paper No(s)/Mail Date *4/12/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This office action is in response to applicant's communication filed on 8/4/10.

Claims 1-16 are pending in this application.

Applicant's election with traverse of Group I, claims 1-12 and 17-18, when the compounds are non heterocyclic compounds in the reply filed on 8/4/10 is acknowledged. The traversal is on the ground(s) that heterocycle/heterocyclyl/heterocycloalkyl and non hetrocyclic compounds should be grouped together and examined because there is common linear backbone. This is not found persuasive because the backbone can change depending from the starting substituent, for example, R1-Y can be starting group, and additionally, there will be undue burden on the USPTO for the examination of the entire scope of claim 1.

The requirement is still deemed proper and is therefore made FINAL.

Claims 1-12 and 17-18 will be examined to the extent they read on the compound being non heterocyclic group. Claims 13-16 are additionally withdrawn from the consideration, being drawn to the non elected group.

Applicant's election of example 40 on page 105 is acknowledged herewith.

Information Disclosure Statement

The information disclosure statement (IDS) submitted on 4/12/06 is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement has been considered by the examiner.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 9-11 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

There has been recited a method of treating a patient who has, or in preventing a patient from getting, a disease or condition selected from the groups consisting of Alzheimer's, for helping prevent or delay the onset of Alzheimer's disease, for treating patients with mild cognitive impairment (MCI) and/or preventing or delaying the onset of Alzheimer's disease in those who would progress from MCI to AD, for treating Down's syndrome, for treating humans who have Hereditary Cerebral Hemorrhage with Amyloidsis of the Dutch-Type, for treating cerebral amyloid angiopathy and/or preventing its potential consequences .....
, or diffuse Lewy body type of Alzheimer's disease and who is in need of such treatment, but the specification is not enabled for such a scope.

A number of factors are relevant to whether undue experimentation would be required to practice the claimed invention, including "(1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims." In re Wands, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988).

(1). Breadth of Claims: Claims 9-11 are directed to a method of treating or preventing a vast array of diseases by administering to a host in need of such treatment a compound of claim 1.

The central characteristic of Alzheimer's disease is the deficiency in the level of the neurotransmitter Acetylcholine that plays an important role in memory or it is believed that too much stimulation of nerve cells by

glutamate may be responsible for the degeneration of nerves that occur in Alzheimer's disease. Like other neurotransmitters, glutamate is produced and released by nerve cells in the brain. The released glutamate then travels to nearby nerve cells where it attaches to a receptor on the surface of the cells called the N-methyl-D-aspartate (NMDA) receptor. Drugs such as memantine blocks the receptor and thereby decreases the effects of glutamate. It is thought that by blocking the NMDA receptor and the effects of glutamate, memantine may protect nerve cells from excess stimulation by glutamate. Thus, Alzheimer's disease can be treated by Acetylcholinesterase inhibitors that reduce the depletion of acetylcholine or by drugs that inhibit NMDA receptor. The skill level in the art is so low that the only treatments available to this day are drugs that inhibit Acetylcholinesterase or drugs that inhibit NMDA receptor that decreases the effects of glutamate. Applicants' compounds do not do this. Thus, the enablement rejection is proper.

Dementia associated with Parkinson's disease is also the same as treating Parkinson's disease, since Parkinson's is associated with dementia. Parkinson's disease is a neurological disorder that is also characterized by rhythmic muscle tremors, hypokinesia, and muscular rigidity. Dopamine, a hormonelike substance is an important neurotransmitter in both the central and peripheral nervous systems that is currently used as treatment for Parkinsonism. Dopamine is a neurotransmitter involved in the regulation of the central nervous system. The skill level in the art is such low that the only treatments available to this day are drugs that are helpful in regulating Dopamine.

Thus, a rejection under 35 U.S.C. 112, first paragraph is proper. There has been recited in claim 9, a method of treating mild cognitive impairment, but the specification is not enabled for such a scope. Cognitive Impairment or disorders - are disorders in a brain that prevents someone from thinking well, from solving problems, or from storing information. Three main types of cognitive disorders are: Delirium, Dementia, and Amnesia.

Dementia is a label for a cluster of symptoms involving deterioration in behaviours such as memory, language, and reasoning. The deterioration results from a disease process in the brain. The disease progresses from mild through severe stages and interferes with the ability to function independently in everyday life. Dementias are fatal medical diseases that have major psychosocial consequences.

Dementia is classified as cortical or subcortical depending on the area of brain affected. *Cortical dementia* causes problems in memory, thinking, and language. Alzheimer's Disease is a disorder that causes cortical dementia. The cognitive problems, depending on their nature, are called aphasia, apraxia, amnesia, and agnosia. These problems may include difficulty finding words, difficulty comprehending written or spoken material, and even mutism. Speech, which is the machinery for sound, is usually normal; however, it is the language component that breaks down. The memory problem is often an inability to learn new information.

Insight into the condition is usually absent and a person's mood is unconcerned or uninhibited. The motor system is normal, at least in the early stages.

Subcortical dementia affects parts of the brain below the cortex and is characterized by slowing, difficulty in retrieving information from memory, and altered mood. Parkinson's disease and multiple sclerosis are examples of a condition that can result in a subcortical dementia. Language ability is usually normal, although speech is dysfunctional and the motor system may result in stooped or extended posture, increased muscle tone, and tremors. Memory problems are due to a difficulty in retrieving information that is in fact learned. The person's mood may be either apathetic or depressed, and insight into the condition is usually present.

Delirium is a condition of severe confusion and rapid changes in brain function, usually the result of treatable physical or mental illness. Acute confusional states are usually the result of a physical or mental illness and are usually temporary and reversible.

Delirium involves a rapid alternation between mental states (for example, from lethargy to agitation and back to lethargy), with attention disruption, disorganized thinking, disorientation, changes in sensation and perception, and other symptoms.

Disorders that cause delirium are numerous and varied. They may include conditions that deprive the brain of oxygen or other substances. Delirium may be caused by diseases of body systems other than the brain, by poisons, by fluid/electrolyte or acid/base disturbances, and by other serious, acute conditions.

Mental retardation - is described as below-average general intellectual function

with associated deficits in adaptive behavior that occurs before age 18. Causes of mental retardation are numerous, but a specific reason for mental retardation is determined in only 25% of the cases. Failure to adapt normally and grow intellectually may become apparent early in life or, in the case of mild retardation, not become recognizable until school age or later. An assessment of age-appropriate adaptive behaviors can be made by the use of developmental screening tests. The failure to achieve developmental milestones is suggestive of mental retardation. A family may suspect mental retardation if motor skills, language skills, and self-help skills do not seem to be developing in a child or are developing at a far slower rate than the child's peers. The degree of impairment from mental retardation has a wide range from profoundly impaired to mild or borderline retardation. Less emphasis is now placed on degree of retardation and more on the amount of intervention and care required for daily life.

Causes of mental retardation can be roughly broken down into several categories: unexplained (This category is the largest and a catchall for undiagnosed incidences of mental retardation.)

trauma (prenatal and postnatal)
infectious (congenital and postnatal)
chromosomal abnormalities

genetic abnormalities and inherited metabolic disorders
metabolic
nutritional

environmental

As shown above, since the origin and nature of cognitive impairments are different one from the other, it is impossible to treat cognitive impairments in general.

Scope of Compounds - The scope of the compounds is broad. It is apparent that hundreds of millions of combinations of compounds can be created from the definitions, owing especially to broad scope of Rc, X, R2, R3, R1, R20 and RN.

(2). Direction of Guidance: The amount of direction or guidance is minimal. No data on any specific compound is given. The dosage is generic and it ranges from 10 fold to about 10,000 fold (see page 45).

(3). State of Prior Art: There is no evidence of record that compounds structurally similar to these benzimidazole compounds are in use for the treatment or prevention of Alzheimer's disease, or the treatment/prevention of other diseases recited in claims 9-11.

(4). Workinq Examples: There is no any working example that indicates the inhibition of Al3-peptide production, which in return is presumed to treat or prevent AD. There is no biological data for any of the compounds.

(5). Nature of the Invention and Predictability: The invention is directed to treat or prevent Alzheimer's disease and is also directed to treat/prevent other diseases recited in claims 9-11. It is well established that "the scope of enablement varies inversely with the degree of unpredictability of the factors involved," and physiological activity is generally considered to be an unpredictable factor. See In re Fisher, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970).

(6). The Relative Skill of Those in the Art: Applicants claim a method of treatment for AD, this is a very hard to treat disease. The central characteristic of Alzheimer's disease is the deficiency in the level of the neurotransmitter Acetylcholine that plays an important role in memory. Alzheimer's disease is an extraordinarily difficult disease to treat, and has been the subject of a vast amount of research. Despite an enormous number of different approaches, the skill level in the art is so low relative to the difficulty of task that the only success has come from treatment by compounds which are Acetylcholinesterase inhibitors (Aricept®, Cognex®, Exelon®, and Reminyl®) a property these compounds are not disclosed to have.

(7). The Quantity of Experimentation Necessary: Immense, especially in view of point 6, since the inhibition of Ai3-peptide production for the treatment of AD has never been accomplished. Thus, no guidance from the success of others is available from this experimentation.

MPEP 2164.01(a) states, "A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation. *In re Wright,* 999 F.2d 1557,1562,

27 USPQ2d 1510, 1513 (Fed. Cir. 1993)." That conclusion is clearly justified here.

In regard to the phrase "preventing a patient from getting, a disease or condition selected from the group consisting of Alzheimer's disease, for helping prevent or delay the onset of Alzheimer's disease...", to this day no one was able to prevent a person from getting Alzheimer's disease. The only means available is the treatment of patients suffering for example from depression or anxiety, but not preventing someone from getting Alzheimer's disease in the first place. Like wise, the same enablement rejection applies for the prevention of other diseases recited in claim 9 (e.g. prevent the 3otential consequences of cerebral amyloid angiopathy).

It is recommended that applicants delete claims 9-11 to overcome this rejection.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 12 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

This claim recites a method for making a compound of claim1, without reciting any steps, thus rendering the claim indefinite.

Claims 17-18 provides for the use of compound, but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

Claims 17-18 are is rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under

35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd.* v. *Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

The elected species is free of prior art and are allowable.

Claims 1-8 are objected to as containing heterocyclic groups, but would be allowable if rewritten in independent form including all of the limitations of the base claim encompassing the elected species and closely related compounds and any intervening claims.

.WO 9118866 is cited to show the state of the art. See examples 12 and 13.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SHAILENDRA KUMAR whose telephone number is (571)272-0640. The examiner can normally be reached on Mon-Fri/5-4-9.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sullivan Daniel can be reached on (571)272-0779. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

S. Kumar
10/7/10

/SHAILENDRA KUMAR/
Primary Examiner, Art Unit 1621